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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|-----------------|-------------|----------------------|---------------------|
|-----------------|-------------|----------------------|---------------------|

08/737,446 01/10/97 DUPRE

J 223/051

HM22/0416

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EXAMINER

NOLAN, P

ART UNIT

PAPER NUMBER

1644

14

DATE MAILED:

04/16/99

Please find below and/or attached an Office communication concerning this application or
proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

08/737,446

Applicant(s)

Dupre

Examiner

Nolan

Group Art Unit

1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Response

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 3-29-99.
- ☐ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 38-47 is/are pending in the application.
- ☐ Of the above claim(s) _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 38-47 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) _____.
- ☐ received in this national stage application from the International Bureau (PCT Rule 1.7.2(a)).

*Certified copies not received: _____.

Attachment(s)

- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☒ Notice of References Cited, PTO-892
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Interview Summary, PTO-413
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Other _____

Office Action Summary

Art Unit: 1644

Part III DETAILED ACTION

1. Claims 38-47 are pending.
2. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.
3. Claims 41 and 46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.
Applicant has no specific support for the species GLP 1 (7-36), in their specification of claims as originally filed. It is suggested Applicant amend their claims to GLP 1 (7-37).

4. Claims 38-41 and 43-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of GLP 1 (7-36) amide or GLP 1 (7-37) in treating Type I diabetes subcutaneously, does not reasonably provide enablement for the use of any analog to GLP 1 (7-36) amide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to use the invention commensurate in scope with these claims.

Claims 38-41 and 43-46 recite the use of an analogue to GLP 1 (7-36) amide to treat Type I diabetes, however, the present specification fails to disclose any other peptide which has GLP 1 (7-36) amide activity in treating diabetes. In addition, the specification provides no guidance as to which of the 30 amino acids may be changed while GLP 1 (7-36) amide activity is retained. The total number of 30 amino acid peptides is 3.4×10^{29} . The number of single amino acid substitutions is 600. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain GLP 1 (7-36) amide activity, and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Ngo et al., (V), newly cited, in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.), it would require an undue amount of experimentation for one of skill in the art to arrive at the other 30 amino acid peptides that have GLP 1 (7-36) amide activity.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not

identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

5. Claims 38-47 are rejected under 35 U.S.C. § 103 as being unpatentable over Gutniak et al. (V), of record, in view of U.S. Patent 5,424,286, of record (A), D'Alessio et al., (W) newly cited and Goth (X), newly cited.

Gutniak et al., teaches the intravenous use of GLP 1(7-36)amide in Type I diabetes, wherein GLP 1(7-36)amide decreased the need for insulin dosage required to maintain euglycemia (see abstract, in particular). Gutniak et al., also teaches that both GLP-1(7-37) and GLP-1(7-36) exerted strong insulinotropic effects in vitro and in vivo (see page 1316, in particular). Lastly Gutniak et al., teaches coadministration of insulin in type I diabetics prior to the feeding of a meal (see page, 1317).

The claimed invention differs from the prior art teachings only by the recitation of treating Type I diabetics with GLP-1(7-36)amide or GLP-1(7-37) subcutaneously. However, in summarizing the use of the Gutniak et al., findings, the '286 patent teaches that "In patients with IDDM (i.e. Type I diabetes), the GLIP (i.e. GLP-1(7-36)amide) treatment lowered the insulin required by one half. This glucose dependent activity is a very desirable characteristic for a therapeutic agent that can be used to treat DM avoiding the complications of hypoglycemic side effects". In addition, D'Alessio et al., also summarized to findings of Gutniak et al., by stating "It has recently been reported that infusions of GLP-1 into diabetic subjects decreased the insulin dosage required to maintain euglycemia. Furthermore, type I diabetic subjects treated with GLP-1 during one step euglycemic, hyperinsulinemic clamps had 10-15% higher rates of glucose than during control studies, thereby suggesting that GLP-1 may promote glucose uptake in addition to augmenting insulin release". Lastly, Goth teaches that when drugs are injected intravenously they are rapidly distributed, but when a prolonged absorption of drugs is desirable, for example in the administration of insulin (which is art recognized as being used to treat Type I diabetes), the subcutaneous route is used.

One of ordinary skill in the art at the time the invention was made would have been motivated to treat Type I diabetics with either GLP-1(7-36)amide or GLP-1(7-37) since both are known to show

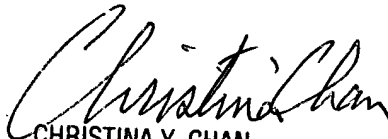
Art Unit: 1644

strong insulinotropic effects in vivo as taught by Gutniak et al., and use a subcutaneous route of administration since the physiological effects of GLP 1 (7-36) amide are insulinotropic, and the prior art teaches coadministration of insulin and GLP 1 (7-36) amide for their combined blood glucose reducing capabilities and Goth teaches that it is desirable to prolong the absorption of insulin by administering it subcutaneously. The results of the Gutniak et al., teachings, when viewed from the point of view of those skilled in the art (i.e. the '286 patent and D'Alessio et al.) would reasonably suggest treating Type I diabetics with GLP-1(7-36)amide or GLP-1(7-37). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick Nolan whose telephone number is (703) 305-1987. The examiner can normally be reached on Monday through Friday from 8:30 am to 4:30 pm.

7. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (703) 305-3973. The FAX number for our group, 1644, is (703) 305-7401. Any inquiry of a general nature relating to the status of this application or proceeding should be directed to the Group receptionist, whose telephone number is (703) 308-0196

Patrick Nolan, Ph.D.
April 15, 1999


CHRISTINA Y. CHAN
SUPERVISORY PATENT EXAMINER
GROUP 1800/1644